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HELLER EHRMAN LLP
275 MIDDLEFIELD ROAD
MENLO PARK, CA 94025-3506

EXAMINER	
KEMMERER, ELIZABETH	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/991,150
Filing Date: November 16, 2001
Appellant(s): BAKER ET AL.

Ginger R. Dreger
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 03 April 2006 appealing from the Office action mailed 16 September 2004.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The following are the related appeals, interferences, and judicial proceedings known to the examiner which may be related to, directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal:

09/941,992 (under final rejection)

09/990,711 (reply brief filed)

(3) Status of Claims

The statement of the status of claims contained in the brief is essentially correct. In the amendment filed 07 January 2004, claim 235 was also amended.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct. Of course, the examiner disagrees with the statements regarding the significant gene amplification of PRO341 in certain cancers for reasons explained herein.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Sen, 2000, Curr. Opin. Oncol. 12:82-88.

Hittelman, 2001, Ann. NY Acad. Sci. 952:1-12.

Pennica et al., 1998, PNAS USA 95:14717-14722.

Konopka et al., 1986, PNAS USA 83:4049-4052.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 124, 129-131, and 135-145 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to isolated nucleic acids comprising the full-length coding sequence of the nucleic acid sequence of SEQ ID NO: 19, or the full-length coding sequence of the cDNA deposited under ATCC accession number 209792. These nucleic acids encode a polypeptide referred to as PRO341. Claims are also presented to vectors and host cells comprising these nucleic acids. Claims are also presented to fragments of these nucleic acids consisting of at least 30 nucleotides or more wherein the fragment hybridizes under defined stringent conditions to the nucleic acid sequence of SEQ ID NO: 19 or the full-length coding sequence of the cDNA deposited under ATCC accession number 209792. The record shows that Appellant relies on an asserted utility of the use of PRO341 nucleic acids as cancer diagnostic agents to meet the requirements of 35 U.S.C. § 101.

At pages 539-555, a gene amplification assay discloses that genomic DNA encoding PRO341 had a ΔCt value of at least 1.0 for three out of fourteen lung tumor samples. Genomic DNA encoding PRO341 was not amplified in any of the fourteen colon tumor samples. At page 548, ΔCt is defined as the threshold PCR cycle, or the cycle at which the reporter signal accumulates above the background level of fluorescence. The specification further indicates that ΔCt is used as "a quantitative measurement of the relative number of starting copies of a particular target sequence in a nucleic acid sample when comparing cancer DNA results to normal human DNA results." It is noted that at page 548, it is stated that samples are used if their values are within 1 Ct of the 'normal standard'. It is further noted that the ΔCt values at pages 550-554 are expressed (a) with values to one one-hundredth of a unit (e.g. 2.58), and (b) that very few values were obtained that were at least 2. Given the paucity of information, the data do not support the implicit conclusion of the specification that PRO341 genomic DNA shows a positive correlation with lung cancer, much less that the levels of PRO341 genomic DNA would be diagnostic of such. Even *if* the data demonstrated a slight increase in copy number of PRO341 genomic DNA in primary tumors, such would not be indicative of a use of the claimed nucleic acids as diagnostic agents. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean that the nucleic acid is a cancer marker, but can merely be an indication that the cancer tissue is aneuploid. Furthermore, the literature

reports that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy *before* the epithelial cells turn cancerous. See Hittelman (2001, Ann. NY Acad. Sci. 952:1-12), who teach that damaged, precancerous lung epithelium is often aneuploid. See especially p. 4, Figure 4. The gene amplification assay in the specification does not provide a direct comparison between the lung tumor samples and normal lung epithelium. Rather, the assay discloses amplification of PRO341 genomic DNA in lung tumors compared to "normal human DNA" (apparently from blood samples), and thus a skilled artisan would not conclude that PRO341 genomic DNA is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium. One skilled in the art would not conclude that PRO341 genomic DNA is a diagnostic probe for lung cancer unless it is clear that PRO341 genomic DNA is amplified to a clearly greater extent in true lung tumor tissue relative to non-cancerous lung epithelium. Also, while it might be argued in hindsight that PRO341 would still be a marker at least for precancerous, or damaged, lung epithelium, such is not suggested by the specification as originally filed and is not well-established in the prior art.

Since the skilled artisan would have to conduct further research to reasonably confirm that PRO341 DNA can be used as a cancer diagnostic agent, the asserted utility is not in currently available form, and is not substantial. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific

> benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Claims 124, 129-131, and 135-145 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(10) Response to Argument

At the middle of p. 4 of the Brief, Appellant argues that the patentable utility of PRO341 nucleic acids is based on the gene amplification data for the gene encoding the PRO341 polypeptide. Appellant states that the specification shows significant amplification of the gene encoding PRO341 in three different lung tumors. Appellant refers to the declaration of Dr. Goddard (submitted under 37 C.F.R. § 1.132 on 07 July 2004) as explaining that a gene that is amplified at least 2-fold by the disclosed gene amplification assay in a tumor sample relative to a normal sample is useful for the diagnosis of cancer, for monitoring cancer development, and/or for measuring the efficacy of cancer therapy. Appellant concludes that one of ordinary skill in the art would find it credible that the claimed PRO341 gene has utility as a marker for the diagnosis of lung tumors. This has been fully considered but is not found to be persuasive for the following reasons. The specification shows that PRO341 genomic DNA was amplified in only three out of fourteen lung tumor samples as compared to a

normal human DNA control that was apparently isolated from blood. One skilled in the art would conclude that it was more likely than not that PRO341 genomic DNA is *not* amplified in any given lung tumor sample based on those results. Furthermore, the data are not based on direct comparison of amplification levels between lung tumor and healthy lung. Comparison of matched tissue samples is considered the standard in the cancer diagnosis art. See Pennica et al. and Konopka et al., (of record in related PRO341 applications), for instance. The Goddard declaration was not found to be sufficient to overcome the rejection; however, the Goddard declaration will be addressed at length later in this answer.

At p. 4 to p. 5 of the Brief, Appellant argues that the Hittelman reference submitted by the examiner supports the Appellant's position that there is utility in identifying genetic biomarkers in epithelial tissues at cancer risk. Appellant argues that even if PRO341 detects precancerous cells, PRO341 is still a precancer marker and therefore has utility. Appellant urges that the skilled artisan would know that early detection of lung cancer provides information in advance about risk assessment, prognosis, and therapy for lung cancer. Appellant concludes that the application discloses at least one patentable utility for the claimed PRO341 gene. This has been fully considered but is not found to be persuasive. The instant specification does not assert that PRO341 can be used as a precancer marker or as a cancer risk determining agent. The specification does not disclose whether PRO341 gene is amplified only in lung tumor, in precancerous lung, or also in healthy lung. Given that proper controls were not done (i.e., comparing gene amplification levels between cancerous and non-

cancerous matched lung tissues), and that PRO341 was positive in only 3 out of 14 lung tumor samples, further research would reasonably be required of the skilled artisan to confirm the utilities asserted in the specification and the Appeal Brief. Such a requirement for further research indicates that the asserted utilities are not substantial.

At the bottom of p. 5 of the Brief, Appellant argues that the PRO341 gene has utility in the diagnosis of lung cancer. Appellant urges that, based on such a utility, the teachings in the art and in the specification, one skilled in the art would know exactly how to use the claimed nucleic acids for the diagnosis of cancer without any undue experimentation. This has been fully considered but is not found to be persuasive. As argued above and below, the claims are rejected under 35 U.S.C. § 101 as not being supported by a substantial asserted utility. Therefore, the claims are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

At pp. 6-8 of the Brief, Appellant reviews the legal standard for utility, with which the examiner takes no issue.

At p. 8 of the Brief, Appellant argues that the data in Example 170 (starting at p. 539 of the specification) describes results of a gene amplification assay. Appellant characterizes the assay as using a well-known and routinely employed PCR assay that is capable of quantitatively measuring the level of gene amplification in a sample. Appellant asserts that gene amplification is an essential mechanism for oncogene

activation. Appellant reviews how the assay was performed, and reports that the gene encoding PRO341 was significantly amplified (2.173-fold to 2.514-fold) in three lung tumors. This has been fully considered but is not found to be persuasive. First, it is important to note that the gene encoding PRO341 was not found to be amplified in eleven out of fourteen lung tumor samples, and also was not found to be amplified in any colon tumor samples. Also, matched tissue samples were not used for controls. Rather, the control DNA appears to have been isolated from blood (bottom of p. 547). The art uses matched tissue samples to determine whether or not a nucleic acid can be used as a cancer diagnostic agent (see Pennica et al., Konopka et al.). Given these details, one skilled in the art would not conclude that the gene encoding PRO341 would be useful as a cancer diagnostic agent or a target for cancer drug development, but would rather view the data as preliminary results.

From p. 8 to p. 9 of the Brief, Appellant refers to the declaration of Dr. Goddard, submitted under 37 C.F.R. § 1.132 on 07 July 2004. Appellant quotes from p. 3 of the declaration as giving an expert opinion that a 2-fold increase in gene copy number in a tumor sample relative to a non-tumor sample is significant and useful. Appellant concludes that one skilled in the art would consider the 2.173 to 2.514-fold amplification of the gene encoding PRO341 in three lung tumors is significant and credible based upon the facts in the Goddard declaration. This has been fully considered but is not found to be persuasive. In assessing the weight to be given expert testimony, the examiner may properly consider, among other things, the nature of the fact sought to be established, the strength of any opposing evidence, the interest of the expert in the

outcome of the case, and the presence or absence of factual support for the expert's opinion. See Ex parte Simpson, 61 USPQ2d 1009 (BPAI 2001), Cf. Redac Int'l. Ltd. v. Lotus Development Corp., 81 F.3d 1576, 38 USPQ2d 1665 (Fed. Cir. 1996), Paragon Podiatry Lab., Inc. v. KLM Lab., Inc., 948 F.2d 1182, 25 USPQ2d 1561, (Fed. Cir. 1993). In the instant situation, the nature of the fact sought to be established is whether or not a 2.173 to 2.514-fold amplification of the gene encoding PRO341 in three lung tumors is significant and credible. Credibility has never been questioned. However, the significance can be questioned since eleven of the fourteen lung tumor samples did not show an amplification of the gene encoding PRO341, and the control used was not a matched non-tumor sample but rather was a DNA sample from blood of healthy subjects. The art uses matched tissue samples (see Pennica et al., Konopka et al.). Pennica et al. and Konopka et al. speak to the strength of the opposing evidence, as does Hittelman and Sen who indicate that gene amplification occurs in non-cancerous tissue because of aneuploidy. The expert has interest in the outcome of the case since Dr. Goddard is listed as an inventor and is employed by the assignee. Finally, the expert refers to three publications as factual support for the conclusions in the declaration. However, none of Livak et al., Heid et al., nor Pennica et al. appear to indicate that an approximately 2-fold amplification of genomic DNA is significant in tumors. The Goddard declaration evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO341 gene has *not* been associated with tumor formation, the development of cancer, the progression of cancer, the prediction of cancer, or the recovery from cancer during treatment. The

specification merely demonstrates that the PRO341 genomic DNA was amplified in some cancers, to a minor degree (about 2.5 fold), relative to normal blood DNA. No mutation or translocation of PRO341 has been associated with any type of cancer versus normal tissue. It is not known whether PRO341 is amplified in corresponding normal tissues, and what the relative levels of amplification are. In the absence of any of the above information, all that the specification does is indicate that the DNA encoding PRO341 may be amplified in a variety of samples and invites the artisan to determine the significance of this increase. The specification presents a mere invitation to experiment. Based on consideration of the evidence as a whole, the rejection is proper.

In the second paragraph of p. 9 of the Brief, Appellant argues that it is well known that gene amplification occurs in most solid tumors, including lung carcinomas, and is generally associated with poor prognosis. Appellant concludes that the PRO341 gene becomes an important diagnostic marker to identify malignant lung carcinomas, even when the lung malignancy associated with PRO341 molecule is a rare occurrence. This has been fully considered but is not found to be persuasive. As discussed in the rejection above, gene amplification is common in non-cancerous lung epithelium based on the damage the epithelium suffers from exposure to the environment. See Sen and Hittelman et al. There is no control for non-cancerous lung tissue, and thus the relevance of the data in the specification is not clear. Furthermore, there is no disclosure of a correlation of amplification with tumor formation, progression, severity, etc., all of which speak to prognosis.

From p. 9 to the top of p. 10 of the Brief, Appellant argues that the asserted utility for PRO341 as a cancer diagnostic is credible and specific. The examiner agrees.

From the middle of p. 10 to the middle of p. 11 of the Brief, Appellant argues that the requirement for an asserted utility to be "substantial" means that the claimed invention must have a "practical purpose" which is not a throw-away or insubstantial use, such as the use of a complex invention as landfill. Appellant quotes from M.P.E.P. § 2107 regarding the requirement for a substantial asserted utility. Appellant argues that they have demonstrated at least one reasonable use for the PRO341 nucleic acid as a diagnostic marker for detecting or at least classifying lung carcinomas. Appellant urges that such uses serve a practical purpose which is not a throw-away or insubstantial use. Appellant also objects to the examiner's characterization of the gene amplification as "preliminary data," stating that the data for PRO341 ad the teachings of the Goddard declaration support the Appellant's position that the PRO341 gene is a tumor marker for certain types of lung tumors. This has been fully considered but is not found to be persuasive. M.P.E.P. § 2107 I states:

> A "substantial utility" defines a "real world" use. Utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use are not substantial utilities.

In the instant case, the asserted utility that PRO341 nucleic acids are useful as diagnostic markers for cancer is not substantial in that further research is required to reasonably confirm a real world context of use. In order for PRO341 nucleic acid to be useful as a cancer diagnostic agent, there must be a detectable change in the amount or form of PRO341 nucleic acid between cancerous and healthy tissue. In the instant

case, the evidence of record indicates that the initial gene amplification assay only showed a positive result for three out of fourteen lung cancer sample, and did not take into account aneuploidy in cancerous and non-cancerous lung tissue (lack of matched tissue sample control, lack of aneuploidy control). In view of this, the skilled artisan would have viewed the gene amplification results as preliminary with respect to the utility of the claimed nucleic acids, and would have had to experiment further to reasonably confirm whether or not PRO341 nucleic acids can be used as a cancer diagnostic agent.

At the bottom of p. 11 to the top of p. 12 of the Brief, Appellant argues that Hittelman studied premalignant lesions and suggested that epithelial tumors develop through a multistep process driven by genetic instability. Appellant states that Hittelman showed that a subset of the same molecular changes found in tumor were also found in premalignant lesions, suggesting that the premalignant lesions might represent precursor lesions for associated tumors. Appellant submits that, contrary to the rejection, the Hittelman reference supports Appellant's position that there is utility in identifying genetic biomarkers in epithelial tissues at cancer risk. Appellant points to Hittelman's statement that it is important to identify individuals at increased risk for developing cancer who might benefit from different types of intervention. Appellant urges that, even if the observed PRO341 amplification were due to chromosomal aneuploidy, identifying genetic markers with this aneuploidy is a very important and useful step in identifying individuals at increased risk of cancer. Appellant concludes that Hittelman supports at least one utility of the claimed PRO341 nucleic acids.

Appellant urges that the skilled artisan would know that early detection of lung cancer provides information about risk assessment, prognosis, and therapy. This has been fully considered but is not found to be persuasive. The instant specification does not assert that PRO341 can be used as a precancer marker or as a cancer risk determining agent. The specification does not disclose whether PRO341 gene is amplified only in lung tumor, or also in precancerous lung, or also in healthy lung. Given that proper controls were not done (i.e., comparing gene amplification levels between cancerous and non-cancerous matched tissues), and that PRO341 was positive in only 3 out of 14 lung tumor samples, further research would reasonably be required of the skilled artisan to confirm the utilities asserted in the specification and the Appeal Brief. Such a requirement for further research indicates that the asserted utilities are not substantial.

At the middle of p. 12 of the Brief, Appellant argues that beta-actin and GAPDH were used as internal controls. Appellant also points to the use of a negative control of pooled DNA isolated from the cells of ten normal healthy individuals. Appellant asserts that the protocols and controls are art accepted. Appellant urges that the same protocols and controls have been used to identify several other tumor markers for various cancers, and that the art and the USPTO have accepted the same protocol and controls as credible. Appellant indicates that several patent applications have been allowed based on the same protocol and controls. Appellant urges that the examiner is applying a heightened utility standard in this instance, which is legally incorrect. This has been fully considered but is not found to be persuasive. The beta-actin and GAPDH controls do not speak to the issue of whether PRO341 is also amplified in non-

cancerous lung tissue. The pooled DNA from ten normal healthy individuals was isolated from blood cells, not lung tissue, and thus does not constitute a matched tissue negative control. There is no evidence to support Appellant's assertion that the art accepts these controls. Finally, each patent application is examined on its own merits. The other patent applications to which Appellant refers may have reported amplification in a higher percentage of tissues tested, or may have disclosed different experimental details, or had other evidence submitted during prosecution.

From p. 12 to p. 13 of the Brief, Appellant argues that the specification shows that the gene encoding PRO341 was significantly amplified 2.173 to 2.514-fold in three lung tumors. Appellant urges that these values were considered significant based on the declaration of Dr. Goddard. Appellant argues that the examiner's characterization of the amplification as "not clear" was without basis or evidence. Appellant argues that the examiner must accept an opinion from a qualified expert. Appellant argues that the fact that 3 out of 14 lung tumor samples tested positive in the gene amplification assay does not make the gene amplification data less significant or spurious. Appellant reasons that some tumor markers are useful for identifying rare malignancies. Appellant argues that such rare tumor markers have great value in tumor diagnosis, prognosis, and classification of tumors. Appellant concludes that it is not relevant to utility whether the PRO341 gene was amplified in three lung tumors or most lung tumors sampled. This has been fully considered but is not found to be persuasive. The gene amplification data presented in the specification were problematic. The control DNA was from blood rather than from a matched tissue sample (i.e., healthy lung), while the literature shows

that matched tissue samples are the standard (Pennica et al., Konopka et al.). Also, the data were not corrected for aneuploidy, a phenomenon that occurs in cancerous and non-cancerous lung (Sen, Hittelman). Therefore, it is not clear that the reported amplification is significant. Furthermore, the three lung tumor samples in which PRO341 was reported as being amplified were not of the same type. PRO341 tested positive in LT16, LT17, and LT21. These are described in the specification as corresponding to stage IB squamous cell carcinoma, stage IIB squamous cell carcinoma, and stage IIB large cell carcinoma, respectively. Other lung tumor samples of the same types did not test positive for PRO341 gene amplification. Therefore, the relevancy of Appellant's comments regarding rare malignancies is not clear. If PRO341 were amplified in all stage IIB squamous cell carcinomas, for example, but no other lung carcinomas, such would appear to indicate that PRO341 was a significant rare malignancy marker for stage IIB squamous cell carcinoma. However, no such trend was disclosed. The specification does not disclose any special feature, or prognosis, of lung tumors that amplify the PRO341 gene compared to lung tumors that do not amplify the PRO341 gene. It is left to the skilled artisan to determine the significance (if any) of such a difference. Such constitutes the type of further research required to bestow a substantial utility on the claimed invention.

Appellant concludes that the rejection is not based on a *prima facie* case of lack of utility. Appellant urges that the rejection should be withdrawn for lack of evidence. Finally, Appellant urges that the claimed invention meets the "substantiality" requirement set forth n the utility guidelines and by the U.S. Supreme Court in Brenner

v. Manson, 383 U.S. 519 (1966). This has been fully considered but is not found to be persuasive. The gene amplification assay disclosed that PRO341 was amplified in three out of fourteen lung tumor samples compared to normal blood DNA. Even *if* the data demonstrated a slight increase in copy number of PRO341 genomic DNA in primary tumors, such would not be indicative of a use of the claimed nucleic acids as diagnostic agents. Cancerous tissue is known to be aneuploid, that is, having an abnormal number of chromosomes (see Sen, 2000, Curr. Opin. Oncol. 12:82-88). The data presented in the specification were not corrected for aneuploidy. A slight amplification of a gene does not necessarily mean that the nucleic acid is a cancer marker, but can merely be an indication that the cancer tissue is aneuploid. Furthermore, the literature reports that lung epithelium is at risk for cellular damage due to direct exposure to environmental pollutants and carcinogens, which result in aneuploidy *before* the epithelial cells turn cancerous. See Hittelman (2001, Ann. NY Acad. Sci. 952:1-12), who teach that damaged, precancerous lung epithelium is often aneuploid. See especially p. 4, Figure 4. The gene amplification assay in the specification does not provide a direct comparison between the lung tumor samples and normal lung epithelium. Rather, the assay discloses amplification of PRO341 genomic DNA in lung tumors compared to "normal human DNA" (apparently from blood samples), and thus a skilled artisan would not conclude that PRO341 genomic DNA is amplified in cancerous lung epithelium more than in damaged (non-cancerous) lung epithelium. One skilled in the art would not conclude that PRO341 genomic DNA is a diagnostic probe for lung cancer unless it is clear that PRO341 genomic DNA is

amplified to a clearly greater extent in true lung tumor tissue relative to non-cancerous lung epithelium. Also, while it might be argued in hindsight that PRO341 would still be a marker at least for precancerous, or damaged, lung epithelium, such is not suggested by the specification as originally filed and is not well-established in the prior art. Since the skilled artisan would have to conduct further research to reasonably confirm that PRO341 DNA can be used as a cancer diagnostic agent, the asserted utility is not in currently available form, and is not substantial. See Brenner v. Manson, 148 U.S.P.Q. 689 (Sup. Ct., 1966), wherein the court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

At p. 14 of the Brief, Appellant argues that the specification discloses the sequence of PRO341 and step-by-step protocols for performing the gene amplification assay. Appellant concludes that the skilled artisan would know how to make and use the claimed nucleic acids for the diagnosis of lung carcinoma. Appellant argues that, based on the disclosure and the advanced state of the art in oncology, the skilled artisan would have found such testing routine and not undue. This has been fully considered but is not found to be persuasive. The examiner concedes that the specification teaches how to make the claimed PRO341 nucleic acids. However, the specification fails to provide a substantial asserted utility for the claimed PRO341

nucleic acids, and thus the specification also fails to enable the claimed PRO341 nucleic acids (specifically, the specification fails to teach the skilled artisan how to use the claimed PRO341 nucleic acids without undue experimentation). As discussed above, PRO341 genomic DNA was found to be amplified in only three out of fourteen lung cancer samples compared to a normal DNA control from blood. Gene amplification in lung tumors was not compared to a matched normal tissue sample, as is the standard in the art (see Pennica et al., Konopka et al.). The data were not corrected for aneuploidy, which was known to be common in cancerous *and non-cancerous* lung tissue (see Sen, Hittelman). Thus, the skilled artisan would have to perform further research to reasonably confirm the real world context of use of PRO341 nucleic acids as cancer diagnostic agents. Such a requirement for further research indicates that the asserted utility is not substantial.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

(12) Oral Hearing

Appellant has not requested an oral hearing. However, in the event that Appellant requests such, the examiner also request the opportunity to present statements at the oral hearing.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

Elizabeth C. Kemmerer, Ph.D.

Elizabeth C. Kemmerer

ELIZABETH KEMMERER
PRIMARY EXAMINER

Conferees:

Janet Andres, Ph.D.

JANET L. ANDRES
SUPERVISORY PATENT EXAMINER

Brenda Brumback

Brenda Brumback

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600